

2001. The Examiner notes that there was no English translation provided by the Applicants. Office Action at page 7. Applicants submit that they complied with the requirements of 37 C.F.R. § 1.98(3)(i) by providing a concise explanation of the relevance of each document not in the English language. See also M.P.E.P. § 609A(3). According to 37 C.F.R. § 1.98(3)(ii), written translations of non-English-language documents need only be submitted where they are "within the possession, custody, or control of, or [are] readily available." For the reasons above, Applicants respectfully request that the Examiner consider the cited foreign patents.

The Amended Claims Are Definite

The Examiner rejected claims 34-38 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention. Office Action at page 3. According to the Examiner, claim 34 (and those claims dependent thereon) recites a functionalized hemiacetal having the general formula as set forth in claim 34, wherein n is 0 or 1. The Examiner alleges that the formula is vague and indefinite because there is no "n" variable recited in the formula.

Applicants thank the Examiner for pointing out the accidental omission of the variable "n" from the formula in claim 34. Applicants have amended claim 34 to provide recitation of "n."

The Examiner also asserts that the phrase "compatible with the reaction carried out" in claim 34 is vague and indefinite because it is allegedly unclear how one skilled in

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the art would be able to ascertain the full scope of compounds that are "compatible with the reaction carried out." *Id.*

According to the M.P.E.P.:

Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art;

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

M.P.E.P. § 2173.02.

Applicants respectfully submit that one of ordinary skill in the art would clearly recognize that the phrase "compatible with the reaction carried out" includes any substituent that does not interfere with the reaction between the polyalkyleneimine and the functionalized hemiacetal. Applicants further submit that one skilled in the art could readily identify such substituents by applying basic principles of organic chemistry. Moreover, the specification provides examples of compatible groups at page 7, lines 20-23.

The Examiner also asserts that the phrase "targeting element" in claim 34 is vague and indefinite because it is allegedly unclear what the element, in this context, is intended to target. Office Action at page 3.

Applicants respectfully submit that the specification clearly informs the skilled artisan that targeting elements are moieties that direct the transfer of functionalized polyalkyleneimine-nucleic acid complexes toward desired cell types, certain desired

tissues, or certain desired cell compartments. See page 6, lines 25-28. Moreover, the specification provides examples of intended targets at, for example, page 7, line 14 through page 8, line 14.

The claims must be read in view of the specification, and "no claim may be read apart from and independent of the supporting disclosure on which it is based." See M.P.E.P. §§ 2173.02-2173.03; see also *In re Cohn*, 438 F.2d 989, 169 U.S.P.Q. 95 (C.C.P.A. 1971). Here, the Examiner is improperly ignoring the definition of "targeting element" in the specification. Applicants submit that one skilled in the art would understand that a targeting element is a moiety that directs the transfer of functionalized polyalkyleneimine-nucleic acid complex toward desired cell types, certain desired tissues, or certain desired cell compartments.

Lastly, with regard to claim 34, the Examiner asserts that there is no antecedent basis for the term "hemiacetyl" in claim 23. Office Action at page 3.

Applicants thank the Examiner for pointing out the spelling error. Applicants have amended claims 34 and 38 to correctly recite "hemiacetal."

For the reasons above, Applicants respectfully request the reconsideration and withdrawal of the rejections of claims 34-38 under 35 U.S.C. § 112, second paragraph.

The Claims Are Not Obvious

The Examiner rejected claims 23-33 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zanta *et al.* in view of Neidigh *et al.* Office Action at pages 4-6.

Applicants respectfully traverse this rejection.

The Examiner asserts that Zanta *et al.* teach a method for functionalization of polyethyleneimine. Office Action at page 5. She acknowledges that the reference fails to disclose the use of titanium (IV) isopropoxide and sodium borohydride in an alcoholic solvent. *Id.* She also acknowledges that Zanta *et al.* do not teach the limitations of dependent claims 27-29. *Id.* To overcome these deficiencies, the Examiner relies on Neidigh *et al.* as teaching the preparation of N-methyl secondary amines by reductive amination of aldehydes or ketones, comprising the treatment of carbonyl compounds with methylamine hydrochloride, triethylamine, and titanium (IV) isopropoxide in absolute ethanol with sodium borohydride as the reducing agent. *Id.* The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time of this application was filed to modify the method for functionalization of polyethyleneimine as allegedly taught by Zanta *et al.* with the conditions for reductive amination allegedly taught by Neidigh *et al.* Office Action at pages 5-6.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, the prior art reference (or references when combined) must teach or suggest all the claim elements. Furthermore, "[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art." See M.P.E.P. § 2143.01, quoting *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a reference or to combine reference teachings. Third, there must be a reasonable expectation of success. See M.P.E.P. § 2143. With regard to dependent claims, "[i]f an independent

claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious." M.P.E.P. § 2143.03, p. 2100-126 citing *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988).

Applicants respectfully submit that the cited references alone, or in combination, fail to teach or suggest all the claim elements. The claims recite a process for making functionalized polyalkyleneimines, wherein a polyalkyleneimine is treated with a functionalized hemiacetal in the presence of titanium (IV) isopropoxide and sodium borohydride in an alcoholic solvent. In contrast, Neidigh *et al.* only disclose a method for making N-methyl secondary amines by reacting an aldehyde or a ketone with a primary amine, triethylamine, and titanium (IV) isopropoxide in the presence of ethanol (followed by treatment of the mixture with sodium borohydride). The claimed process is clearly distinguishable in that there is no aldehyde or ketone as a starting material. In addition, triethylamine is not used in the claimed process.

Moreover, there is no teaching or suggestion in the references that the method of Neidigh *et al.* is useful for coupling hemiacetals, especially functionalized hemiacetals with other reactive groups, to polyalkyleneimines. Nor has the Examiner provided any evidence that one skilled in the art would have a reasonable expectation of success in (1) leaving out triethylamine or (2) using Neidigh's disclosed reaction conditions to couple a functionalized hemiacetal to a polyalkyleneimine.

Instead, the Examiner appears to suggest that the invention is obvious simply because individual reagents and synthetic steps for making other compounds were known in the art. Applicants assert, however, that "[v]irtually all inventions are

necessarily combinations of old elements." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 961 (Fed. Cir. 1983). Indeed, "[o]nly God works from nothing. Men must work with old elements." *Fromson v. Advanced Offset Plate, Inc.*, 755 F.2d 1549, 1556 n.3, 225 U.S.P.Q. 26, 31 n.3 (Fed. Cir. 1985).

In summary, the cited prior art references (1) fail to teach or suggest all the claim elements when taken alone or together, (2) fail to provide suggestion or motivation to modify or combine teachings, and (3) fail to provide a reasonable expectation of success. Rather, the Examiner has impermissibly used Applicants' own specification to provide a blueprint for combining prior art elements. See *In re Dembiczak*, 50 U.S.P.Q.2d 1614 (Fed. Cir. 1999). Therefore, Applicants respectfully submit that the Examiner has failed to make a *prima facie* case of obviousness. At best, the Examiner has proposed an "obvious to try" scenario that is not a proper basis for an obviousness rejection.

For the reasons above, Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 23-33 under U.S.C. § 103(a).

Conclusion

In view of the foregoing amendments and remark, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

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Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: March 24, 2003

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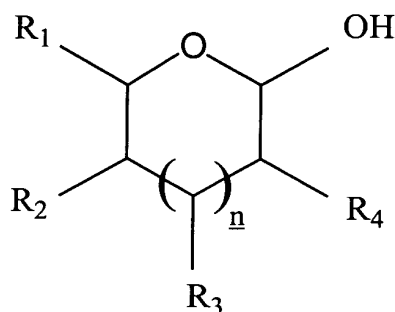
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APPENDIX TO AMENDMENT OF MARCH 24, 2003
VERSION WITH MARKINGS TO SHOW CHANGES MADE

Deleted text is marked by double strikethrough, and added text is underlined.

Amendments to the Claims

34. (Amended) The process according to claim 23, wherein the functionalized ~~hemiacetyl~~ hemiacetal has the general formula:



wherein n is 0 or 1;

R₁, R₂, R₃, and R₄ are independently hydrogen, a group compatible with the reaction carried out, or a targeting element; and

only one of R₁, R₂, R₃, and R₄ is a targeting element.

38. (Amended) The process according to claim 37, wherein between about 1% and about 20% of the functionalized ~~hemiacetyl~~ hemiacetal is grafted onto the polyalkyleneimine.